Remarks

Applicants request re-consideration of the above-referenced patent application.

I. Amendments to the Specification

In accordance with 37 CFR §1.78 and MPEP §202.01, we have (1) updated the first paragraph of the specification with the patent number for the parent patent, and (2) corrected the filing date of U.S. Provisional Application No. 60/241,633.

II. Amendments to the Claims

This amendment cancels claim 7 without prejudice to its patentability, and adds claims 8-13. Thus, claims 1-6 and 8-13 are pending. Claims 1-6 have been amended. The pending claims, including the amendments, are shown in the previous section. Applicants submit that the amendments and new claims do not introduce new matter. Specifically:

Claim 1 has been amended to replace "Y'" with "Y^1" in accordance with the Examiner's suggestion in Paragraph 5(d) of the Office action.

Claim 1 has been amended to replace "fused aryl" with "naphthyl". This amendment is supported by Applicants' specification at, for example, page 22, lines 12-14.

Claims 1 and 3 have been amended to remove "keto" from various substituent definitions.

Claims 1 and 3 have been amended to replace "aryl" with "phenyl". This amendment is supported by Applicants' specification at, for example, page 20, lines 22-24.

Claims 2 and 3 have been amended to remove Formula I. This removes a redundancy, given that claim 1 (*i.e.*, the claim from which claims 2 and 3 depend) also defines the compounds as corresponding in structure to Formula I.

Claims 2, 3, 5, and 6 have been amended to expressly recite isomers, enantiomers, tautomers, racemates, and polymorphs of the recited compounds. This amendment makes the language of these claims more consistent with the language of claim 1.

Claim 4 has been amended to replace the "-CO-H-CH_2-CO-NH-" linker with a "-CO-NH-CH_2-CO-NH-" linker. This amendment corrects an obvious error (as recognized in Paragraph 5(g) of the Office action), and is therefore permissible under MPEP §2163.07. In addition, the amendment is supported by, for example, Applicants' generic description of their compounds, as well as the specific examples illustrating the preparation of such compounds.

Claim 5 has been amended to additionally recite the presence of a pharmaceutically acceptable carrier in the composition. This amendment is supported by Applicants' specification at, for example, page 19, lines 7-15; and page 32, lines 28-31.

Claim 6 has been amended to replace the phrase "a condition mediated by the $\alpha_v\beta_3$ or $\alpha_v\beta_5$ integrin" with the phrase "a condition treatable by inhibiting or antagonizing $\alpha_v\beta_3$ or $\alpha_v\beta_5$ integrin". This amendment is supported by Applicants' specification at, for example, page 11, line 28 to page 12, line 4; and page 19, lines 7-13.

Claim 6 has been amended to identify conditions being treated by the method. This amendment is supported by Applicants' specification at, for example, claim 7 (as originally filed).

New claims 8, 10, and 12 are supported by, for example, claim 5 (as originally filed). Specifically, originally-filed claim 5 is a multiple dependent claim. These multiple dependencies have simply been separated into amended claim 5, new claim 8, new claim 10, and new claim 12. Claims 8, 10, and 12 also include the amendments discussed above with respect to claim 5.

New claims 9, 11, and 13 are supported by, for example, claim 6 (as originally filed). Specifically, originally-filed claim 6 is a multiple dependent claim. These multiple dependencies have simply been separated into amended claim 6, new claim 9, new claim 11, and new claim 13. Claims 9, 11, and 13 also include the amendments discussed above with respect to claim 6.

Other amendments simply rephrase the claims, remove redundancies or unnecessary terms, or correct grammatical or obvious errors. Applicants submit that such amendments do not affect the scope of the claims, and are permissible under MPEP §2163.07.

Applicants reserve the right to pursue any canceled subject matter and/or any other subject matter disclosed in this application in one or more later-filed divisional and/or continuation applications.

III. Update of priority claim

In accordance with 37 CFR §1.78 and MPEP §202.01, we have (1) updated the first paragraph of the specification with the patent number for the parent patent, and (2) corrected the filing date of U.S. Provisional Application No. 60/241,633. Applicants believe these are the only necessary revisions. Applicants ask the Examiner to notify the Undersigned if the Examiner believes the first paragraph may require further revision.

IV. Rejection of claims 1-7 under the judicially-created double patenting doctrine

Claims 1-7 have been rejected under the judicially-created double patenting doctrine in view of U.S. Patent No. 6,720,327. Claims 1-7 also have been provisionally rejected under the judicially-created double patenting doctrine in view of U.S. Patent Application No. 10/381,834. Applicants submit that these rejections are premature because the claims in the present application have not yet been found to be otherwise allowable. Applicants will file a terminal disclaimer (to the extent necessary) once the claims have been found to be otherwise allowable.

V. Rejection of claims 1 and 3-7 in View of U.S. Patent No. 6,028,223

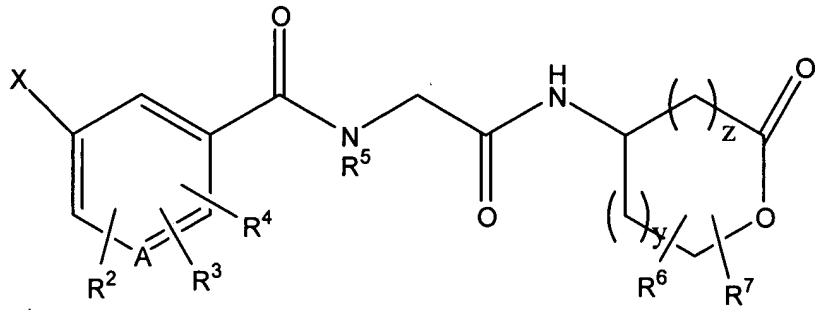
Claims 1 and 3-7 have been rejected under 35 U.S.C. 102(e) in view of U.S. Patent No. 6,028,223 and its parent provisional application (U.S. Provisional Application No. 60/003,277). Applicants request withdrawal of this rejection. Applicants have canceled claim 7, thereby mooting this rejection as to that claim. As to claims 1 and 3-6 (and new claims 8-13), Applicants submit that the subject matter is patentable over the cited references for at least the following reasons:

A. Claim 1

In support of the rejection, the Office action specifically points to the compound of Example N in column 68; the compounds of Examples 188-191 in columns 173-174; an intermediate in Example 226 in column 193, line 45-68; an intermediate in Example 362 in column 299, lines 15-30; an intermediate in Example 393 in column 316; an intermediate in Example 394 in column 318; an intermediate in Example 399 in column 320, lines 20-43; intermediates in Examples 407-414 in columns 324-326; and intermediates in Examples 453-460 in columns 343-345 of U.S. Patent No. 6,028,223.

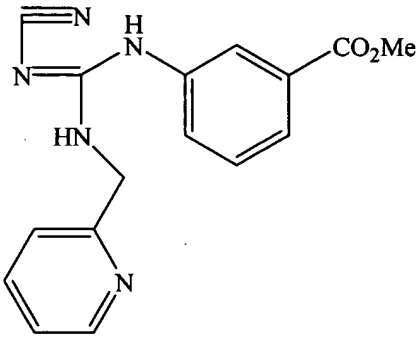
At the outset, Applicants note that Example N of U.S. Patent No. 6,028,223 is the only example cited by the Office action that is expressly included in the cited provisional application. Thus, to the extent the Office action relies on the provisional application for this rejection, the none of the other cited examples should be considered. *See, e.g.*, MPEP §2136.03(III). Applicants can provide a copy of U.S. Provisional Application No. 60/003,277 upon request from the Examiner.

Claim 1 is directed to lactone compounds corresponding generally to the following structure:



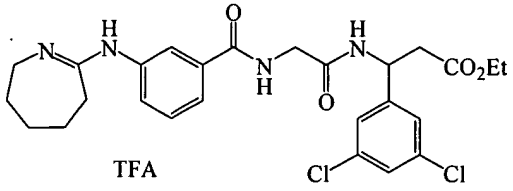
In this structure, R^6 and R^7 are independently selected substituents.

In contrast to claim 1, Example N of U.S. Patent No. 6,028,223 discusses the following compound:



As can be seen, this compound does not fall within the genus recited in claim 1. This compound, for example, is not a lactone.

Examples 188-191 discuss the following compounds:



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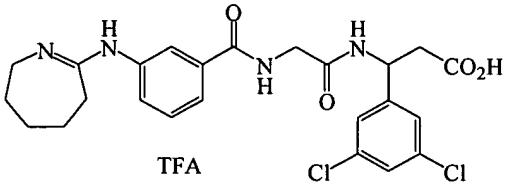

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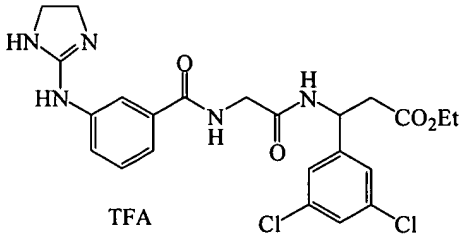

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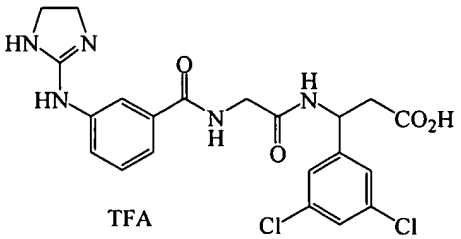
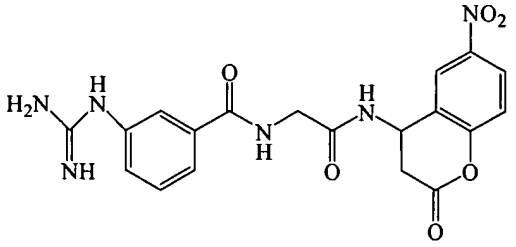


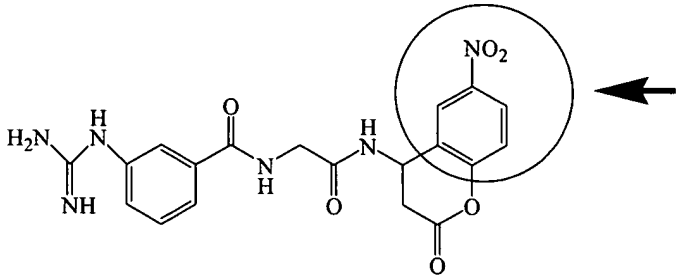
TFA

As can be seen, these compounds do not fall within the genus recited in claim 1. These compounds, for example, are not lactones.

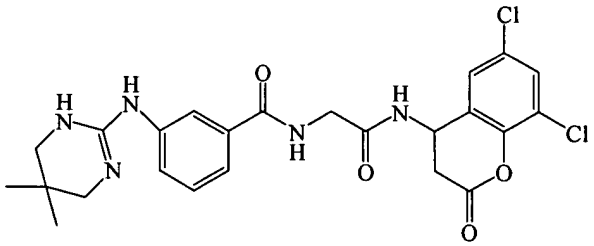
The cited intermediate in Example 226 is believed to correspond in structure to the following formula:



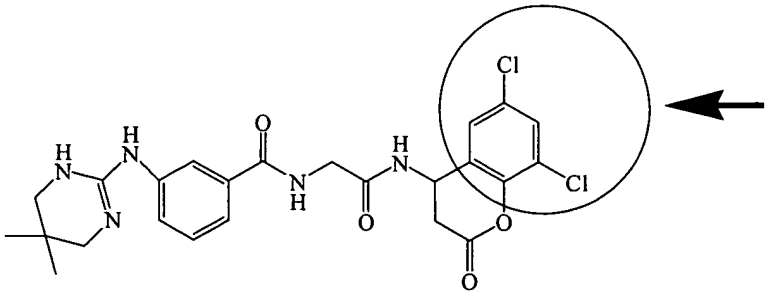
This compound does not satisfy the definitions of R^6 and R^7 in Applicants' claim 1. More specifically, R^6 and R^7 in Applicants' claim 1 are independent substituents, and therefore cannot together form a nitro-substituted phenyl ring (*i.e.*, R^6 and R^7 cannot form the ring circled below):



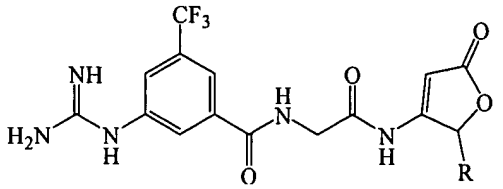
The cited intermediate in Example 362 is believed to correspond in structure to the foliowing formula:



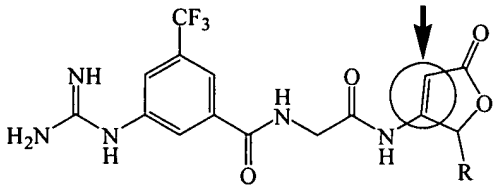
Like the compound of Example 226, this compound does not satisfy the definitions of R^6 and R^7 in Applicants' claim 1. More specifically, R^6 and R^7 in Applicants' claim 1 are independent substituents and therefore cannot together form a chloro-substituted phenyl ring (*i.e.*, R^6 and R^7 cannot form the ring circled below):



The cited intermediates in Examples 393, 394, 399, 407-414, and 453-460 are believed to correspond generally to the following formula:



These compounds do not fall within Applicants' claim 1. In contrast to the lactone ring in Applicants' claim 1, the lactone rings in these examples have a double bond (*i.e.*, the bond circled in the structure below):



B. Claims 3-6 and 8-13

Claims 3, 5, and 6 depend from claim 1, and are therefore novel over the cited references for at least the same reasons as claim 1.

Claim 4 is directed to species having a single-ring lactone with no double bonds between the ring atoms. Thus, claim 4 is patentable over the cited references for at least the same reasons as claim 1. New claims 12 and 13 depend from claim 4, and are therefore novel over the cited references for at least the same reasons as claim 4.

New claims 8 and 9 depend from claim 2. The Office action did not reject claim 2 in view of the cited art, thus indicating that claim 2 is patentable over the art. New claims 8 and 9 are patentable over the art for at least the same reasons as claim 2.

New claims 10 and 11 also depend from claim 3, and are therefore novel over the cited references for at least the same reasons as claim 3.

VI. Rejection of claims 1 and 3-7 in View of WO 97/08145

Claims 1 and 3-7 have been rejected under 35 U.S.C. 102(a) in view of WO 97/08145. Applicants request withdrawal of this rejection. Applicants have canceled claim 7, thereby mooting this rejection as to that claim. As to claims 1 and 3-6 (and new claims 8-13), Applicants submit that the subject matter is patentable over WO 97/08145 for at least the same reasons

discussed above with respect to U.S. Patent No. 6,028,223. After all, the examples in WO 97/08145 cited by the Office action are the same as those cited by the Office action with respect to U.S. Patent No. 6,028,223.

VII. Rejection of claims 1-7 under the second paragraph of 35 U.S.C. §112

Claims 1-7 have been rejected under the second paragraph of 35 U.S.C. §112. Applicants request withdrawal of this rejection. Applicants have canceled claim 7, thereby mooting this rejection as to that claim. As to claims 1 and 3-6 (and new claims 8-13), Applicants submit the following in support of their request for withdrawal of this rejection:

In Paragraph 5(a), the Office action objects to the use of "aryl" in claim 1 in view of the definition in the specification, which includes heteroaryls in addition to non-heteroaryl rings. To expedite prosecution of this application, Applicants have replaced "aryl" with "phenyl", and "fused aryl" with "naphthyl". Applicants, however, make no representation as to the merit of the Office action's objection.

In Paragraph 5(b), the Office action objects to claim 1 because some substituents are themselves defined as being optionally substituted. Applicants submit that there is no prohibition under 35 U.S.C. §112 against defining a substituent as a substituted moiety. In the instant case, claim 1 expressly defines each substituent, as well as any optional substituents thereof. One skilled in the art would understand such language. Thus, the language particularly points out and distinctly claims the invention, and therefore satisfies 35 U.S.C. §112.

In Paragraph 5(c), the Office action objects to Markush groups in claim 1 as being redundant for listing both an optionally-substituted substituent and the unsubstituted substituent itself. Per the Examiner's request, we have amended the claim 1 to remove this redundancy.

In Paragraph 5(d), the Office action objects to the use of "Y'" in claim 1. As the Examiner suggested, we have amended the claim to replace "Y'" with "Y^1".

In Paragraph 5(e), the Office action objects to the use of "keto" in claim 1. To expedite prosecution of this application, Applicants have removed that term. Applicants, however, make no representation as to the merit of the Office action's objection.

In Paragraph 5(f), the Office action objects to the punctuation of the phrase "and all isomers, enantiomers, tautomers or polymorphs thereof" in claim 1. Applicants submit that the amendments to claim 1 have mooted this objection.

In Paragraph 5(g), the Office action objects to several compounds in claim 4 for having a -CO-H-CH_2-CO-NH- linker. As the Office action indicates, the divalent "H" is an obvious error. As requested by the Office action, we have fixed the structures to replace the linker with a -CO-NH-CH_2-CO-NH- linker.

In Paragraph 5(h), the Office action objects to the multiple dependencies of claims 5 and 6. Applicants have separated the dependencies into different claims such that claims 5 and 6 depend only from claim 1, new claims 8 and 9 depend only from claim 2, claims 10 and 11 depend only from claim 3, and new claims 12 and 13 depend only from claim 4. Applicants have made this amendment to expedite prosecution of this application, and make no representation as to the merit of this rejection.

In Paragraph 5(i), the Office action objects to claim 5 for not reciting any component in the composition beyond Applicants' compound. Applicants submit that the Office action is improperly requiring claim 5 to be enabling by requiring claim 5 to recite additional components. More specifically, it is the purpose of the specification --- not the claims --- to enable one skilled in the art to practice the invention. The function of the claims, in contrast, is to simply define the metes and bounds of the invention:

> The purpose of claims is not to explain the technology or how it works, but to state the legal boundaries of the patent grant. A claim is not "indefinite" simply because it is hard to understand when viewed without the benefit of the specification.

S3 Inc. v. Nvidia Corp., 259 F.3d 1364, 1369, 59 U.S.P.Q.2d 1745, 1748 (Fed. Cir. 2001). *See, also, Application of Johnson*, 558 F.2d 1008, 1017, 194, U.S.P.Q. 187 (Cust. & Pat. App. 1977) ("One does not look to the claims to find out how to practice the invention they define, but to the specification."). In the instant case, the specification fulfills its purpose of enabling the compositions recited in the claims. And claim 5 fulfills its sole purpose of defining the metes and bounds of the invention, *i.e.*, a pharmaceutical composition comprising a compound recited in claim 1. There certainly is no requirement for a composition claim to recite the exact make-up of the composition. At most, only critical features or essential ingredients of a composition must be recited. *See, e.g.*, MPEP §§2164.08(c) & 2172.01. Thus, claim 5 is proper, and the rejection should be withdrawn. Nevertheless, in an effort to expedite prosecution of this application,

Applicants have amended claim 5 to additionally recite the presence of a pharmaceutically-acceptable carrier in accordance with the Examiner's request.

In Paragraph 5(j), the Office action objects to the phrase "a condition mediated" in claim 6. Applicants submit that the amendments to claim 6 have mooted this objection. Specifically, the amendments to claim 6 have removed the phrase-in-question, and characterize the condition as being treatable by inhibiting or antagonizing $\alpha_v\beta_3$ or $\alpha_v\beta_5$ integrin.

In Paragraph 5(j), the Office action also objects to claim 6 for not reciting an exact step or process of administration. Applicants submit that the Office action is improperly requiring claim 6 to be enabling by requiring claim 6 to recite such steps. As noted above, it is the purpose of the specification --- not the claims --- to enable one skilled in the art to practice the invention. The function of the claims, in contrast, is to simply define the metes and bounds of the invention. In the instant case, the specification fulfills its purpose of enabling the method recited in the claims. *See, e.g.*, pages 32-35. And claim 6 fulfills its sole purpose of defining the metes and bounds of the invention, *i.e.*, administering a therapeutically-effective amount of a compound recited in claim 1. Thus, claim 6 is proper, and the objection should be withdrawn.

In Paragraph 5(k), the Office action objects to claims 2 and 3 for being dependent on rejected claim 1. As noted above, Applicants submit that the rejections of claim 1 should be withdrawn, thus obviating this objection.

The language of new claims 8, 10, and 12 tracks the language of claim 5. Thus, claims 8, 10, and 12 satisfy the second paragraph of 35 U.S.C. §112 for at least the same reasons as claim 5.

The language of new claims 9, 11, and 13 tracks the language of claim 6. Thus, claims 9, 11, and 13 satisfy the second paragraph of 35 U.S.C. §112 for at least the same reasons as claim 6.

VIII. Rejection of claims 6 and 7 under the first paragraph of 35 U.S.C. §112

Claims 6 and 7 have been rejected under the first paragraph of 35 U.S.C. §112. Applicants request withdrawal of this rejection. Applicants have canceled claim 7, thereby mooting this rejection as to that claim. As to claim 6, Applicants have amended claim 6 to recite specific diseases being treated. The Office action indicates that such a description alone does not satisfy the first paragraph of 35 U.S.C. §112 to the extent any of the listed diseases are not

treatable by inhibiting $\alpha_v\beta_3$ or $\alpha_v\beta_5$ integrin. The amendments to claim 6 moot this concern. Specifically, amended claim 6 expressly requires that the treated condition be treatable by inhibiting or antagonizing $\alpha_v\beta_3$ or $\alpha_v\beta_5$ integrin. Thus, the diseases listed in claim 6 are only covered by claim 6 to the extent that they are treatable by inhibiting or antagonizing $\alpha_v\beta_3$ or $\alpha_v\beta_5$ integrin. The metes and bounds of this claim are therefore clear, concise, and exact. This is particularly true, given the Applicants' detailed description relating to methods of treatment, which provides, for example, details related to useful salts, dosages, routes of administration, and pharmaceutical compositions. *See, e.g.*, Applicants' specification at, for example, 31-35.

New claims 9, 11, and 13, which also are directed to methods-of-treatment, are patentable for at least the same reasons as claim 6.

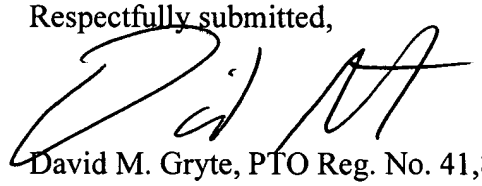
* * * * * * * * *

In view of the foregoing amendments and remarks, Applicants submit that the claims are in condition for allowance.

Applicants hereby request a 3-month extension to reply to the May 11, 2004 Office action, and have enclosed a check to cover that fee. Applicants do not believe that they owe any other fee in connection with this filing. If, however, Applicants do owe any such fee(s), the Commissioner is hereby authorized to charge that fee(s) to Deposit Account No. **08-0750.** In addition, if there is ever a deficiency or overpayment under 37 C.F.R. §1.16 or 1.17 in connection with this patent application, the Commissioner is hereby authorized to charge such deficiency or overpayment to Deposit Account No. **08-0750**.

The Examiner is requested to call the undersigned if any questions arise that can be addressed over the phone to expedite examination of this application.

Respectfully submitted,



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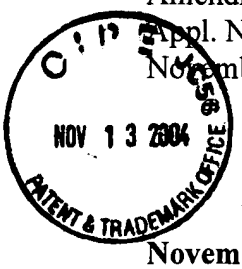
Marked-up Version of Amendments to Specification

The paragraph bridging lines 2-4 on page 1 (as amended in Applicants' November 19, 2003 Amendment A) has been amended in the following manner:

This application is a divisional application of **U.S. Patent No. 6,720,327 (issued April 13, 2004; filed as** U.S. application Ser. No. 09/963,926 **on ~~, filed~~** September 26, 2001**)**, ~~**now allowed,**~~ which claimed priority under Title 35, United States Code §119 of United States Provisional Applications **Ser. No. ~~Ser.No.~~** 60/235,617**,** filed September 27, 2000**,** and Ser. No**.** 60/241,633, filed October **[[10]] 19**, 2000, both now abandoned.



CERTIFICATE OF MAILING UNDER 37 CFR § 1.8

I certify that this correspondence is being deposited with the U.S. Postal Service on **November 12, 2004** with sufficient postage as first class mail (including Express Mail per MPEP §512), and addressed to **Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450**.

DMG/PML